Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	16512	IL NEAR2 ("1" or "2" or "3" or "4" or "5" or "6" or "9")	USPAT	OR	OFF	2005/04/27 15:01
L2	5977852	vector or vector system or cloning system or expression constructs	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L3	1133494	cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L4	5725	"hematopoietic stem cells"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L5	1270912	ligand binding domain or protein binding domain or selective proliferation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L6	233418	steroid hormone receptor	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L7	4509	(vector or vector system or cloning system or expression constructs) and (cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells" and (ligand binding domain or protein binding domain or selective proliferation) and (steroid hormone receptor)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L8	178758	((vector or vector system or cloning system or expression constructs) and (cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells" and (ligand binding domain or protein binding domain or selective proliferation) and (steroid hormone receptor)) and cytokine receptor	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L9	4346	"ligand binding domain"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01

L10	137	("ligand binding domain" same "steroid hormone receptor") and (cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L11	856461	"fusion protein" same proliferat? activity	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L12	13145	"fusion protein" same (proliferat? activity)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L13	3573	((vector or vector system or cloning system or expression constructs) same ("fusion protein" same proliferat? activity)) and "ligand binding domain"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L14	236	((((vector or vector system or cloning system or expression constructs) same ("fusion protein" same proliferat? activity)) and "ligand binding domain") and "hematopoietic stem cells") and "hematopoietic stem cells"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L15	236	((((vector or vector system or cloning system or expression constructs) same ("fusion protein" same proliferat? activity)) and "ligand binding domain") and "hematopoietic stem cells") and (cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L16	6518	"chimeric protein"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L17	5113	"ligand binding domain" or "signal transduction domain" or "protein binding domain"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L18	2289	(cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells"	USPAT	OR	OFF	2005/04/27 15:01
L19	2018	((cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells") and (cytoplasmic domain same ligand binding domain)	USPAT	OR	OFF	2005/04/27 15:01

L20	1730	(((cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells") and (cytoplasmic domain same ligand binding domain)) and (G-CSF or estrogen receptor)	USPAT	OR	OFF	2005/04/27 15:01
L21	1649	(((cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells") and (cytoplasmic domain same ligand binding domain)) and (G-CSF and estrogen receptor)	USPAT	OR	OFF	2005/04/27 15:01
L22	1725	(((cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells") and (cytoplasmic domain same ligand binding domain)) and (G-CSF receptor and estrogen receptor)	USPAT	OR	OFF	2005/04/27 15:01
L23	0	((((cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells") and (cytoplasmic domain same ligand binding domain)) and (G-CSF receptor and estrogen receptor)) and "estrogen receptor ligand binding domain"	USPAT	OR	OFF	2005/04/27 15:01
L24	363294	vector or plasmid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/27 15:01
L25	58343	(fusion or chimer$) WITH protein	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/27 15:01
L26	297	"ligand binding domain" WITH steroid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/27 15:01
L27	14763	cytokine WITH receptor	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/27 15:01
L28	67394	"cell proliferation" or (proliferation WITH cell)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/27 15:01

L29	8470	"hormone receptor"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L30	2874	"cytokine receptor"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L31	41551	"cell proliferation"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L32	62119	cell WITH proliferat$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L33	48714	(fusion or chimer$) NEAR3 (protein or construct)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L34	25124	"binding domain"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L35	13335	G-CSF or (granulocyte WITH stimulat$)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L36	6267	estrogen NEAR3 receptor	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L37	113375	ozawa.in. or itoh.in. or sakata.in. or hasegawa.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L38	144	"hormone receptor" SAME "cytokine receptor"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L39	66	("hormone receptor" SAME "cytokine receptor") and "cell proliferation"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L40	66	(("hormone receptor" SAME "cytokine receptor") and "cell proliferation") and (cell WITH proliferat$)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01

L41	48	((("hormone receptor" SAME "cytokine receptor") and "cell proliferation") and (cell WITH proliferat$)) and ((fusion or chimer$) NEAR3 (protein or construct))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L42	20238	(stem or hematopoietic) NEAR2 cell	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L43	138	"ligand binding domain" same "steroid hormone receptor"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L44	7	("ligand binding domain" same "steroid hormone receptor") and "hematopoietic stem cells"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L45	56	("fusion protein" same (proliferat? activity)) and (("ligand binding domain" same "steroid hormone receptor") and (cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L46	236	(((vector or vector system or cloning system or expression constructs) same ("fusion protein" same proliferat? activity)) and "ligand binding domain") and "hematopoietic stem cells"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L47	236	((((vector or vector system or cloning system or expression constructs) same ("fusion protein" same proliferat? activity)) and "ligand binding domain") and "hematopoietic stem cells") and (cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L48	741	"chimeric protein" and ("ligand binding domain" or "signal transduction domain" or "protein binding domain")	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L49	337	("chimeric protein" and ("ligand binding domain" or "signal transduction domain" or "protein binding domain")) and "cell proliferation"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L50	2	"stimulating factor" with "cytoplasmic domain"	USPAT	OR	OFF	2005/04/27 15:01

L51	15	"stimulating factor" same "cytoplasmic domain"	USPAT	OR	OFF	2005/04/27 15:01
L52	1706	((((cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase)) and "hematopoietic stem cells") and (cytoplasmic domain same ligand binding domain)) and (G-CSF receptor and estrogen receptor)) and (estrogen receptor with ligand binding domain)	USPAT	OR	OFF	2005/04/27 15:01
L53	16	(vector or plasmid) and ((fusion or chimer$) WITH protein) and ("ligand binding domain" WITH steroid) and (cytokine WITH receptor) and ("cell proliferation" or (proliferation WITH cell))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/27 15:01
L54	3	(ozawa.in. or itoh.in. or sakata.in. or hasegawa.in.) and "hormone receptor" and "cytokine receptor"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L55	3	("hormone receptor" SAME "cytokine receptor") SAME "cell proliferation"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L56	41	((((("hormone receptor" SAME "cytokine receptor") and "cell proliferation") and (cell WITH proliferat$)) and ((fusion or chimer$) NEAR3 (protein or construct))) and "binding domain"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L57	31	(("hormone receptor" SAME "cytokine receptor") and "cell proliferation") and ((stem or hematopoietic) NEAR2 cell)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L58	2	"5686281".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L59	32368	(IL NEAR2 ("1" or "2" or "3" or "4" or "5" or "6" or "9")) and (cell proliferation and (G-CSF or estrogen receptor or c-Ab1 or tyrosine kinase))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L60	144	("hormone receptor" SAME "cytokine receptor") and (steroid hormone receptor)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01

L61	0	((("hormone receptor" SAME "cytokine receptor") and (steroid hormone receptor)) and ("fusion protein" same proliferat? activity)) and ((((vector or vector system or cloning system or expression constructs) same ("fusion protein" same proliferat? activity)) and "ligand binding domain") and "hematopoietic stem cells")	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L62	127	(("hormone receptor" SAME "cytokine receptor") and (steroid hormone receptor)) and ("fusion protein" same proliferat? activity)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L63	127	((("hormone receptor" SAME "cytokine receptor") and (steroid hormone receptor)) and ("fusion protein" same proliferat? activity)) and (steroid hormone receptor)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L64	127	((("hormone receptor" SAME "cytokine receptor") and (steroid hormone receptor)) and ("fusion protein" same proliferat? activity)) and (cytokine WITH receptor)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L65	2	"5747292".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L66	2	"6416998".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L67	0	"6416998".pn. and "cytokine receptor"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L68	0	"6416998".pn. and "proliferation domain"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L69	2	"5837544".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L70	1	"5837544".pn. and cytokine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01

L71	138	("ligand binding domain" same "steroid hormone receptor") and steroid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L72	1	("5837544".pn. and cytokine) and steroid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L73	7614	"dual vector" or "binary vector" or "multiple vector" or "cotransformation" or "cotransfection"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L74	115	("dual vector" or "binary vector" or "multiple vector" or "cotransformation" or "cotransfection") and (steroid hormone receptor) and "cytokine receptor"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L75	100	(("dual vector" or "binary vector" or "multiple vector" or "cotransformation" or "cotransfection") and (steroid hormone receptor) and "cytokine receptor") and ((fusion or chimer$) WITH protein)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L76	100	((("dual vector" or "binary vector" or "multiple vector" or "cotransformation" or "cotransfection") and (steroid hormone receptor) and "cytokine receptor") and ((fusion or chimer$) WITH protein)) and (ligand binding domain or protein binding domain or selective proliferation)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L77	19445	"exogenous gene" or "target gene"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L78	26	((((("dual vector" or "binary vector" or "multiple vector" or "cotransformation" or "cotransfection") and (steroid hormone receptor) and "cytokine receptor") and ((fusion or chimer$) WITH protein)) and (ligand binding domain or protein binding domain or selective proliferation)) and ("exogenous gene" or "target gene")	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01

L79	14	nick.IN. and "regulatory elements"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L80	4	"5359046".pn. or "5837544".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L81	1	L80 and "CSF"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L82	4	"5359046".pn. or "5837544".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L83	0	L82 and "cotransformation"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L84	0	L82 and "co-transformation"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:01
L85	2874	"cytokine receptor"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:23
L86	1053	"binding domain" WITH (hormone or estrogen)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:24
L87	43	l85 and l86 and l33	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:24
L88	29	l87 and ("granulocyte colony stimulating factor" or "G-CSF" or "GM-CSF")	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:25
L89	2028	l29 and "cell proliferation"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:25
L90	18	l88 and "cell proliferation"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/27 15:25

	Document ID	Title
1	US 20050074865 A1	Adzymes and uses thereof
2	US 20040115629 A1	Molecules for diagnostics and therapeutics
3	US 20040081648 A1	Adzymes and uses thereof
4	US 20040081647 A1	Adzymes and uses thereof
5	US 20040072271 A1	Target specific screens and their use for discovering small organic molecular pharmacophores
6	US 20040071655 A1	Binding agent
7	US 20040048253 A1	Molecules for diagnostics and therapeutics
8	US 20040014087 A1	Molecules for diagnostics and therapeutics
9	US 20030166161 A1	Gene that imparts selective proliferative activity
10	US 20030152921 A1	Full-length human cDNAs encoding potentially secreted proteins
11	US 20030092057 A1	TARGET SPECIFIC SCREENS AND THEIR USE FOR DISCOVERING SMALL ORGANIC MOLECULAR PHARMACOPHORES
12	US 20030064053 A1	Multivalent protein conjugate with multiple ligand-binding domains of receptors

	Document ID	Title
13	US 20020137699 A1	EXPRESSION SYSTEMS COMPRISING CHIMERIC PROMOTERS WITH BINDING SITES FOR RECOMBINANT TRANSCRIPTION FACTORS
14	US 20020102604 A1	Full-length human cDNAs encoding potentially secreted proteins
15	US 20020004583 A1	Gene that imparts selective proliferation activity
16	US 20020004582 A1	Gene that imparts selective proliferation activity
17	US 6265174 B1	Methods and compositions for identifying and modulating ctionprotein-interactions
18	US 6010861 A	Target specific screens and their use for discovering small organic molecular pharmacophores

	Document ID	Title
1	US 20030235860 A1	Interactions between AR, ER, TR2, and TR4
2	US 6265174 B1	Methods and compositions for identifying and modulating ctionprotein-interactions
3	US 6140120 A	Regulated transcription of targeted genes and other biological events
4	US 6063625 A	Regulated transcription of targeted genes and other biological events
5	US 6046047 A	Regulated transcription of targeted genes and other biological events
6	US 6043082 A	Regulated transcription of targeted genes and other biological events
7	US 6011018 A	Regulated transcription of targeted genes and other biological events
8	US 5869337 A	Regulated transcription of targeted genes and other biological events
9	US 5830462 A	Regulated transcription of targeted genes and other biological events

	Document ID	Title
1	US 20050059073 A1	Method and materials relating to novel stem cell growth factor-like polypeptides and polynucleotides
2	US 20040024725 A1	Regulated apoptosis
3	US 20030044792 A1	Methods and materials relataing to novel stem cell growth factor-like polypeptides and polynucleotides
4	US 6824973 B2	Method of promoting stem cell proliferation or survival by contacting a cell with a stem cell factor-like polypeptide
5	US 6316418 B1	Regulated apoptosis
6	US 6265174 B1	Methods and compositions for identifying and modulating ctionprotein-interactions
7	US 6165787 A	Regulated transcription of targeted genes and other biological events
8	US 6140120 A	Regulated transcription of targeted genes and other biological events
9	US 6063625 A	Regulated transcription of targeted genes and other biological events
10	US 6054436 A	Regulated apoptosis
11	US 6046047 A	Regulated transcription of targeted genes and other biological events

	Document ID	Title
12	US 6043082 A	Regulated transcription of targeted genes and other biological events
13	US 6011018 A	Regulated transcription of targeted genes and other biological events
14	US 5994313 A	Regulated apoptosis
15	US 5972899 A	Apoptosis induced by Shigella IpaB
16	US 5871753 A	Regulated transcription of targeted genes and other biological events
17	US 5869337 A	Regulated transcription of targeted genes and other biological events
18	US 5834266 A	Regulated apoptosis
19	US 5830462 A	Regulated transcription of targeted genes and other biological events

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 FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 15:03:06 ON 27 APR 2005
L1         68245 S (FUSION OR CHIMER?) (2W) (CONSTRUCT OR PEPTIDE OR PROTEIN OR
L2             0 S "CYTOKINE RECEPTOR" (S) "HORMONE BINDING DOMAIN"
L3             3 S "CYTOKINE RECEPTOR" (P) "HORMONE BINDING DOMAIN"
L4             1 DUP REM L3 (2 DUPLICATES REMOVED)
L5          8058 S "CYTOKINE RECEPTOR"
L6           531 S "CYTOKINE RECEPTOR FAMILY"
L7          1594 S "HORMONE BINDING DOMAIN"
L8          1412 S "ESTROGEN" (S) "BINDING DOMAIN"
L9           170 S L1 AND L5
L10           14 S L1 AND L6
L11          161 S L1 AND L7
L12          217 S L1 AND L8
L13            1 S L9 AND L11
L14       292294 S ROBERTS?/AU OR ITO?/AU OR OZAWA?/AU OR CAPON?/AU
L15            4 S L14 AND L9
L16            0 S L14 AND L10
L17            5 S L14 AND L11
L18           11 S L14 AND L12
L19            4 DUP REM L15 (0 DUPLICATES REMOVED)
L20            1 S L19 NOT PY>=1999
L21            3 DUP REM L17 (2 DUPLICATES REMOVED)
L22            2 S L21 NOT PY>=1999
L23           73 S L9 NOT PY>=1999
L24            8 S L10 NOT PY>=1999
L25          113 S L11 NOT PY>=1999
L26          112 S L12 NOT PY>=1999
L27           51 DUP REM L23 (22 DUPLICATES REMOVED)
L28            4 DUP REM L24 (4 DUPLICATES REMOVED)
L29           48 DUP REM L25 (65 DUPLICATES REMOVED)
L30           42 DUP REM L26 (70 DUPLICATES REMOVED)
L31           51 S L27 OR L28
L32           64 S L29 OR L30
L33            0 S L31 AND L32
L34            0 S L27 AND L29
L35            0 S L28 AND L30
L36       262206 S CELL (2W) PROLIFERATION
L37            7 S L36 AND L31
L38            6 S L36 AND L32
L39            7 DUP REM L37 (0 DUPLICATES REMOVED)
L40            6 DUP REM L38 (0 DUPLICATES REMOVED)

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L40 ANSWER 1 OF 6 MEDLINE on STN
ACCESSION NUMBER: 1998250787 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9582373
TITLE: An analysis of Mek1 signaling in **cell proliferation** and transformation.
AUTHOR: Greulich H; Erikson R L
CORPORATE SOURCE: Department of Molecular and Cellular Biology, Harvard University, Cambridge, Massachusetts 02138, USA.. heidi@biosun.harvard.edu
CONTRACT NUMBER: CA42580 (NCI)
F32 GM19098 (NIGMS)
SOURCE: Journal of biological chemistry, (1998 May 22) 273 (21) 13280-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625

AB The Mek1 dual specificity protein kinase phosphorylates and activates the mitogen-activated protein kinases Erk1 and Erk2 in response to mitogenic stimulation. The molecular events downstream of Mek and Erk necessary to promote cell cycle entry are largely undefined. In order to study signals emanating from Mek independent of upstream proteins capable of activating multiple signaling pathways, we fused the **hormone-binding domain** of the **estrogen** receptor (ER) to the C terminus of constitutively activated Mek1 phosphorylation site mutants. Although 4-OH-tamoxifen stimulation of NIH-3T3 cells expressing constitutively activated Mek-ER resulted in only a small increase in specific activity of the **fusion protein**, a 5-10 fold increase in total cellular Mek activity was observed over a period of 1-2 days due to an accumulation of **fusion protein**. Induction of constitutively activated Mek-ER in NIH-3T3 cells resulted in accelerated S phase entry, proliferation in low serum, morphological transformation, and anchorage independent growth. Endogenous Erk1 and Erk2 were phosphorylated with kinetics similar to the elevation of Mek-ER activity. However, elevated Mek-ER activity attenuated subsequent stimulation of Erk1 and Erk2 by serum. 4-OH-tamoxifen stimulation of Mek-ER-expressing fibroblasts also resulted in up-regulation of cyclin D1 expression and down-regulation of p27(Kip1) expression, establishing a direct link between Mek1 and the cell cycle machinery.

L40 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 97265390 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9111327
TITLE: Induction of **cell proliferation** in quiescent NIH 3T3 cells by oncogenic c-Raf-1.
AUTHOR: Kerkhoff E; Rapp U R
CORPORATE SOURCE: Institut fur Medizinische Strahlenkunde und Zellforschung, University of Wurzburg, Germany.
SOURCE: Molecular and cellular biology, (1997 May) 17 (5) 2576-86.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19980206
Entered Medline: 19970515

AB The c-Raf-1 kinase is activated by different mitogenic stimuli and has been shown to be an important mediator of growth factor responses. Fusion of the catalytic domain of the c-Raf-1 kinase with the **hormone binding domain** of the **estrogen** receptor

(deltaRaf-ER) provides a hormone-regulated form of oncogenic activated c-Raf-1. We have established NIH 3T3 cells stably expressing a c-Raf-1 deletion mutant-estrogen receptor **fusion protein** (c-Raf-1-BxB-ER) (N-BxB-ER cells). The transformed morphology of these cells is dependent on the presence of the estrogen antagonist 4-hydroxytamoxifen. Addition of 4-hydroxytamoxifen to N-BxB-ER cells arrested by density or serum starvation causes reentry of these cells into **cell proliferation**. Increases in the cell number are obvious by 24 h after activation of the oncogenic c-Raf-1 protein in confluent cells. The onset of proliferation in serum-starved cells is further delayed and takes about 48 h. In both cases, the proliferative response of the oncogenic c-Raf-1-induced **cell proliferation** is weaker than the one mediated by serum and does not lead to exponential growth. This is reflected in a markedly lower expression of the late-S- and G2/M-phase-specific cyclin B protein and a slightly lower expression of the cyclin A protein being induced at the G1/S transition. Oncogenic activation of c-Raf-1 induces the expression of the heparin binding epidermal growth factor. The Jnk1 kinase is putatively activated by the action of the autocrine growth factor. The kinetics of Jnk1 kinase activity is delayed and occurs by a time when we also detect DNA synthesis and the expression of the S-phase-specific cyclin A protein. This finding indicates that oncogenic activation of the c-Raf-1 protein can trigger the entry into the cell cycle without the action of the autocrine growth factor loop. The activation of the c-Raf-1-BxB-ER protein leads to an accumulation of high levels of cyclin D1 protein and a repression of the p27Kip1 cyclin-dependent kinase inhibitor under all culture conditions tested.

L40 ANSWER 3 OF 6 MEDLINE on STN
ACCESSION NUMBER: 95129555 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7828599
TITLE: B-**cell proliferation** and induction of early G1-regulating proteins by Epstein-Barr virus mutants conditional for EBNA2.
AUTHOR: Kempkes B; Spitkovsky D; Jansen-Durr P; Ellwart J W; Kremmer E; Delecluse H J; Rottenberger C; Bornkamm G W; Hammerschmidt W
CORPORATE SOURCE: Institut fur Klinische Molekularbiologie und Tumorgenetik, Munchen, Germany.
SOURCE: EMBO journal, (1995 Jan 3) 14 (1) 88-96.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950307
Last Updated on STN: 19950307
Entered Medline: 19950217

AB Infection of primary B-lymphocytes by Epstein-Barr virus (EBV) leads to growth transformation of these B-cells in vitro. EBV nuclear antigen 2 (EBNA2), one of the first genes expressed after EBV infection of B-cells, is a transcriptional activator of viral and cellular genes and is essential for the transforming potential of the virus. We generated conditional EBV mutants by expressing EBNA2 as **chimeric fusion protein** with the **hormone binding domain** of the **estrogen** receptor on the genetic background of the virus. Growth transformation of primary normal B-cells by mutant virus resulted in estrogen-dependent lymphoblastoid cell lines expressing the **chimeric** EBNA2 **protein**. In the absence of estrogen about half of the cells enter a quiescent non-proliferative state whereas the others die by apoptosis. EBNA2 is thus required not only for initiation but also for maintenance of transformation. Growth arrest occurred at G1 and G2 stages of the cell cycle, indicating that functional EBNA2 is required at different restriction points of the cell cycle. Growth arrest is reversible for G1/G0 cells as indicated by the sequential accumulation and modification of cell cycle regulating proteins. EBV induces the same cell cycle

regulating proteins as polyclonal stimuli in primary B-cells. These data suggest that EBV is using a common pathway for B-cell activation bypassing the requirement for antigen, T-cell signals and growth factors.

L40 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:119957 BIOSIS
DOCUMENT NUMBER: PREV199698692092
TITLE: Proliferation control of mammalian cells by the tumor suppressor IRF-1.
AUTHOR(S): Koester, Mario; Kirchhoff, Sabine; Schaper, Fred; Hauser, Hansjorg [Reprint author]
CORPORATE SOURCE: Genetics Eukaryotes, GBF-Gesellschaft Biotechnologische Forschung mbh, Mascheroder Weg 1, 38124 Braunschweig, Germany
SOURCE: Cytotechnology, (1995) Vol. 18, No. 1-2, pp. 67-75. ISSN: 0920-9069.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Mar 1996
Last Updated on STN: 27 Mar 1996

AB We have attempted to establish a system in which **cell proliferation** is controlled by a physiological regulator. Interferon regulatory factor 1 (IRF-1) is a transcription factor that recognizes a sequence which is present in the interferon-beta promoter as well as in the promoters of interferon-inducible genes. IRF-1 acts as a tumor suppressor. Constitutive overexpression of recombinant IRF-1 leads to inhibition of cell growth. The extent of this growth arrest depends on the intracellular concentration of IRF-1. In order to allow IRF-1 expression in various mammalian cells we have established two different systems for conditional IRF-1 transcription and activation, respectively. In one case, an inducible promoter, in the other case a **fusion protein** composed of IRF-1 and the **hormone-binding domain** of the human **estrogen** receptor was used. Both systems allow to control gradually the growth of mammalian cell lines by adjusting the intracellular concentration of IRF-1 via estradiol or tetracycline in the medium. Despite the activity of IRF-1 as an antiproliferative agent the expression of certain proteins is retained. Moreover, expression of genes which are controlled by IRF-1 responsive promoters is enhanced.

L40 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 94022353 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8415687
TITLE: Modulation of **cell proliferation** and gene expression by a p53-estrogen receptor hybrid protein.
AUTHOR: Roemer K; Friedmann T
CORPORATE SOURCE: Center for Molecular Genetics, University of California, San Diego, La Jolla 92093-0634.
CONTRACT NUMBER: CA58317 (NCI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Oct 15) 90 (20) 9252-6. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931119

AB We report that p53her, a **chimeric protein** consisting of the complete human wild-type p53 and the human **estrogen** receptor **hormone-binding domain**, strongly suppresses proliferation and induces characteristic morphological changes in Saos-2 human osteosarcoma cells when induced by 17 beta-estradiol. In contrast, p53her constitutively transactivates a p53-responsive promoter in transfection assays, so that transactivation is not regulated by estradiol. However, coexpression of p53her and oncoprotein MDM-2, which

associates with and presumably inactivates p53, results in suppression of p53her-mediated transactivation in the absence, but not the presence, of estradiol. Similarly, p53her induces expression of an endogenous MDM-2 transcript only in the presence of estradiol. These results suggest a correlation between the growth suppressor function of p53her and release of a transactivation block mediated by MDM-2.

L40 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 93309449 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8321220
TITLE: Proliferative activation of quiescent Rat-1A cells by delta FosB.
AUTHOR: Nakabeppu Y; Oda S; Sekiguchi M
CORPORATE SOURCE: Department of Biochemistry, Kyushu University, Fukuoka, Japan.
SOURCE: Molecular and cellular biology, (1993 Jul) 13 (7) 4157-66. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199307
ENTRY DATE: Entered STN: 19930813
Last Updated on STN: 19970203
Entered Medline: 19930730

AB Fos and Jun transcription factors are induced during the normal course of the proliferative response of quiescent cells to serum or to growth factors. We have shown that delta FosB, an alternatively spliced form of FosB, is formed as rapidly as FosB in serum-stimulated Rat-1A cells. Although delta FosB lacks the C-terminal region of FosB carrying the transactivation function, constitutive expression of delta FosB transforms Rat-1A cells as does expression of FosB. The transforming ability of delta FosB suggests that delta FosB may lead to proliferative activation of quiescent cells without activating AP-1-responsive genes. To address this question, FosB or delta FosB was expressed as a **fusion protein** with the ligand **binding domain** of the human **estrogen** receptor (ER) in Rat-1A cells. After estrogen treatment, the **fusion protein** accumulates in nuclei and forms stable complexes with Jun proteins. We have shown that ER-delta FosB or to a lesser extent ER-FosB triggers quiescent Rat-1A cells to transit G1, initiate DNA replication, and ultimately undergo cell division at least once. Since ER-FosB, but not ER-delta FosB, induced expression of the AP-1-responsive transin/stromelysin gene, we concluded that the N-terminal region and the DNA binding domain of FosB or delta FosB itself have the potential to regulate **cell proliferation** and that the transactivation function carried by the C-terminal region of FosB is not essential for the proliferative activation of quiescent cells.

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L39 ANSWER 1 OF 7 MEDLINE on STN
ACCESSION NUMBER: 1999060129 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9843570
TITLE: Activation and functional analysis of Janus kinase 2 in BA/F3 cells using the coumermycin/gyrase B system.
AUTHOR: Mohi M G; Arai K i; Watanabe S
CORPORATE SOURCE: Department of Molecular and Developmental Biology, Institute of Medical Science, University of Tokyo, Tokyo 108-8639, Japan.
SOURCE: Molecular biology of the cell, (1998 Dec) 9 (12) 3299-308. Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990204

AB Janus kinase 2 (Jak2) protein tyrosine kinase plays an important role in interleukin-3- or granulocyte-macrophage colony-stimulating factor-mediated signal transduction pathways leading to **cell proliferation**, activation of early response genes, and inhibition of apoptosis. However, it is unclear whether Jak2 can activate these signaling pathways directly without the involvement of **cytokine receptor** phosphorylation. To investigate the specific role of Jak2 in the regulation of signal transduction pathways, we generated gyrase B (GyrB)-Jak2 fusion proteins, dimerized through the addition of coumermycin. Coumermycin induced autophosphorylation of GyrB-Jak2 fusion proteins, thus bypassing receptor activation. Using different types of chimeric Jak2 molecules, we observed that although the kinase domain of Jak2 is sufficient for autophosphorylation, the N-terminal regions are essential for the phosphorylation of Stat5 and for the induction of short-term **cell proliferation**. Moreover, coumermycin-induced activation of Jak2 can also lead to increased levels of c-myc and CIS mRNAs in BA/F3 cells stably expressing the Jak2 **fusion protein** with the intact N-terminal region. Conversely, activation of the chimeric Jak2 induced neither phosphorylation of Shc or SHP-2 nor activation of the c-fos promoter. Here, we showed that the GyrB-Jak2 system can serve as an excellent model to dissect signals of receptor-dependent and -independent events. We also obtained evidence indicating a role for the N-terminal region of Jak2 in downstream signaling events.

L39 ANSWER 2 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97370080 EMBASE
DOCUMENT NUMBER: 1997370080
TITLE: Discovery of a novel thrombopoietin mimic agonist peptide.
AUTHOR: Kimura T.; Kaburaki H.; Miyamoto S.; Katayama J.; Watanabe Y.
CORPORATE SOURCE: T. Kimura, Research and Development Division, Hokuriku Seiyaku Co. Ltd., Inokuchi, Katsuyama, Fukui 911, Japan
SOURCE: Journal of Biochemistry, (1997) Vol. 122, No. 5, pp. 1046-1051.
Refs: 24
ISSN: 0021-924X CODEN: JOBIAO
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 971218
Last Updated on STN: 971218

AB A random phage peptide library was constructed for the filamentous bacteriophage fuse5. The library was made by inserting a degenerate

oligonucleotide which encodes 15 variable amino acids into the NH2-terminal region of the phage gene III protein. This library, containing 1 X 109 different phages, was screened with a human immunoglobulin **fusion protein** containing the extracellular region of human thrombopoietin receptor. Several phages were isolated following foul cycles of enrichment and amplification. These phages specifically bound to the **fusion protein**. One phage peptide acted as an agonist of the thrombopoietin receptor, since it stimulated the proliferation of thrombopoietin-dependent cells and the differentiation of mouse bone marrow cells to megakaryocytes. The amino acid sequence of this peptide is not present in the primary amino acid sequence of thrombopoietin. This discovery may lead to the design of a small-molecular mimic of thrombopoietin.

L39 ANSWER 3 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96250123 EMBASE
DOCUMENT NUMBER: 1996250123
TITLE: An epidermal growth factor receptor/Jak2 tyrosine kinase domain chimera induces tyrosine phosphorylation of Stat5 and transduces a growth signal in hematopoietic cells.
AUTHOR: Nakamura N.; Chin H.; Miyasaka N.; Miura O.
CORPORATE SOURCE: First Dept. of Internal Medicine, Tokyo Medical and Dental University, 1-5-45 Yushima,Bunkyo-ku, Tokyo 113, Japan
SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 32, pp. 19483-19488.
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 961021
Last Updated on STN: 961021

AB The Jak family of tyrosine kinases and the Stat family of transcription factors have been implicated in transducing signals from the hematopoietic growth factor receptors. To explore the role played by a member of the Jak family, Jak2, in hematopoietic cell growth signaling, we constructed a chimeric cDNA coding for the Jak2 tyrosine kinase domain linked to the extracellular and transmembrane regions of the epidermal growth factor (EGF) receptor (EGFR) and expressed the chimera in an interleukin (IL)-3-dependent cell line, 32D. When deprived of IL-3, EGF prevented apoptosis of the transfected cells, induced dose-dependent proliferation, and supported long- term growth. EGF stimulation of the transfectants induced dose-dependent tyrosine phosphorylation of the EGFR/Jak2 chimera and Stat5, which correlated with the EGF dose dependence of **cell proliferation**. On the other hand, EGF did not induce tyrosine phosphorylation of other factors implicated in **cytokine receptor** signaling, including the IL-3 receptor β subunit, Jak kinases, Stat proteins other than Stat5, Shc, Syp, and mitogen-activated protein kinases. These results suggest that the activation of Jak2 may be sufficient for transducing a growth signal in hematopoietic cells by activating the Stats pathway or previously unidentified signaling pathways. In addition, because EGF induces homodimerization of the EGFR to activate its tyrosine kinase activity, the present study, which shows EGF-dependent activation of the EGFR/Jak2 chimera, implies that Jak2 may also become activated by homodimerization.

L39 ANSWER 4 OF 7 MEDLINE on STN
ACCESSION NUMBER: 96111968 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8777726
TITLE: Herpesvirus Saimiri encodes a new cytokine, IL-17, which binds to a novel **cytokine receptor**.
AUTHOR: Yao Z; Fanslow W C; Seldin M F; Rousseau A M; Painter S L; Comeau M R; Cohen J I; Spriggs M K
CORPORATE SOURCE: Immunex Corporation, Seattle, Washington 98101, USA.
CONTRACT NUMBER: AR41053 (NIAMS)
HG00734 (NHGRI)

SOURCE: Immunity, (1995 Dec) 3 (6) 811-21.
Journal code: 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U31993
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960924
Last Updated on STN: 19990129
Entered Medline: 19960916

AB Herpesvirus Saimiri gene 13 (HVS13) exhibits 57% identity with the predicted sequence of a T cell-derived molecule termed CTLA8. Recombinant HVS13 and CTLA8 stimulate transcriptional factor NF-kappa B activity and interleukin-6 (IL-6) secretion in fibroblasts, and costimulate T **cell proliferation**. An HVS13.Fc **fusion protein** was used to isolate a cDNA encoding a novel receptor that also binds CTLA8. This receptor is unrelated to previously identified **cytokine receptor** families. A recombinant soluble receptor inhibited T **cell proliferation** and IL-2 production induced by PHA, concanavalin A (conA), and anti-TCR MAb. These results define CTLA8 and HVS13 as novel cytokines that bind to a novel **cytokine receptor**. We propose to call these molecules IL-17, vIL-17, and IL-17R, respectively.

L39 ANSWER 5 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95309143 EMBASE
DOCUMENT NUMBER: 1995309143
TITLE: Review of megakaryoblastic cell lines. Characteristic biological features of human megakaryoblastic leukaemia cell lines.
AUTHOR: Hassan H.T.; Freund M.
CORPORATE SOURCE: Department Haematology and Oncology, University Hannover Medical School, Konstanty-Gutschow-Strasse 8,30625 Hannover, Germany
SOURCE: Leukemia Research, (1995) Vol. 19, No. 9, pp. 589-594.
ISSN: 0145-2126 CODEN: LEREDD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 951111
Last Updated on STN: 951111

AB Both normal and leukaemic human megakaryocytopoiesis are stimulated by several cytokines, including stem cell factor, granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin-3, GM-CSF/interleukin-3 **fusion protein**, interleukin-6, interleukin-11, basic fibroblast growth factor and thrombopoietin, but a reinhibited by tumour necrosis factor-alpha, platelet factor 4, beta-thromboglobulin, thrombin, interleukin-4, interferon-alpha and interferon-gamma. Human megakaryoblastic leukaemia cell lines have common biological features, including high expression of the megakaryocytic specific antigen: CD41; high expression of the early myeloid antigens: CD34 and CD33; constitutive expression of interleukin-6 and platelet-derived growth factor; complex karyotype picture; expression of c-kit: the stem cell factor receptor; growth-dependency or -stimulation by stem cell factor, interleukin-3 and/or GM-CSF; megakaryoblastic differentiation by phorbol-myristate-acetate; and in vivo tumorigenicity in mice is associated with marked fibrosis. Only a few agents including phorbol-myristate-acetate; vitamin D3, interferon-alpha, interferon-beta2, erythropoietin and thrombin have been reported to induce megakaryocytic differentiation in the human megakaryoblastic leukaemia cells.

L39 ANSWER 6 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 94020790 EMBASE
DOCUMENT NUMBER: 1994020790
TITLE: Ligand-induced activation of chimeric receptors between the erythropoietin receptor and receptor tyrosine kinases.
AUTHOR: Ohashi H.; Maruyama K.; Liu Y.-C.; Yoshimura A.
CORPORATE SOURCE: Cancer Research Institute, Faculty of Medicine, Kagoshima University, 8-35-1 Sakuragaoka,Kagoshima 890, Japan
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994) Vol. 91, No. 1, pp. 158-162.
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 940206
Last Updated on STN: 940206

AB Ligand-induced dimerization is a key step in the activation of receptor tyrosine kinases, including the epidermal growth factor receptor, stem cell factor receptor (c-kit), and colony-stimulating factor 1 receptor (c-fms). The erythropoietin receptor (EPOR), a member of the **cytokine receptor family**, contains no kinase motif and its activation mechanism remains unclear. Here we show that chimeric receptors carrying the extracellular domain of the epidermal growth factor receptor or c-kit linked to the cytoplasmic domain of the EPOR, transmitted epidermal growth factor or stem **cell** factor-dependent **proliferation** signals in an interleukin 3-dependent cell line. The chimeric receptors as well as the wild-type EPOR also mediated the ligand-induced tyrosine phosphorylation of a set of similar proteins. Moreover, erythropoietin triggered mitogenic signals of chimeric receptors carrying the extracellular domain of the EPOR linked to the tyrosine kinase of c-fms. These data demonstrate the interchangeability of domains between two distinct receptor families and suggest that ligand-induced dimerization is a key step in activating the EPOR.

L39 ANSWER 7 OF 7 EMBASE
on STN
ACCESSION NUMBER: 93218327 EMBASE
DOCUMENT NUMBER: 1993218327
TITLE: Murine c-mpl: A member of the hematopoietic growth factor receptor superfamily that transduces a proliferative signal.
AUTHOR: Skoda R.C.; Seldin D.C.; Chiang M.-K.; Peichel C.L.; Vogt T.F.; Leder P.
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Genetics, Harvard Medical School,Boston, MA 02115, United States
SOURCE: EMBO Journal, (1993) Vol. 12, No. 7, pp. 2645-2653.
ISSN: 0261-4189 CODEN: EMJODG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 930822
Last Updated on STN: 930822

AB The murine myeloproliferative leukemia virus has previously been shown to contain a fragment of the coding region of the c-mpl gene, a member of the **cytokine receptor** superfamily. We have isolated cDNA and genomic clones encoding murine c-mpl and localized the c-mpl gene to mouse chromosome 4. Since some members of this superfamily function by transducing a proliferative signal and since the putative ligand of mpl is unknown, we have generated a chimeric receptor to test the functional potential of mpl. The chimera consists of the extracellular domain of the human interleukin-4 receptor and the cytoplasmic domain of mpl. A mouse

hematopoietic cell line transfected with this construct proliferates in response to human interleukin-4, thereby demonstrating that the cytoplasmic domain of mpl contains all elements necessary to transmit a growth stimulatory signal. In addition, we show that 25-40% of mpl mRNA found in the spleen corresponds to a novel truncated and potentially soluble isoform of mpl and that both full-length and truncated forms of mpl protein can be immunoprecipitated from lysates of transfected COS cells. Interestingly, however, although the truncated form of the receptor possesses a functional signal sequence and lacks a transmembrane domain, it is not detected in the culture media of transfected cells.

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CUMENT NUMBER: 1997349209
TITLE: Development of a novel selective amplifier gene for controllable expansion of transduced hematopoietic cells.
AUTHOR: Ito K.; Ueda Y.; Kokubun M.; Urabe M.; Inaba T.; Mano H.; Hamada H.; Kitamura T.; Mizoguchi H.; Sakata T.; Hasegawa M.; Ozawa K.
CORPORATE SOURCE: Dr. K. Ozawa, Department of Molecular Biology, Institute of Hematology, Jichi Medical School, 3311-1 Yakushiji, Kawachi-gun, Tochigi 329-04, Japan. kozawa@ms.jichi.ac.jp
SOURCE: Blood, (1997) Vol. 90, No. 10, pp. 3884-3892.
Refs: 36
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
025 Hematology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 971230
Last Updated on STN: 971230

AB To overcome the low efficiency of gene transfer into hematopoietic cells, we developed a novel system for selective expansion of transduced cells. To this end, we constructed a chimeric cDNA (GCRER) encoding the **fusion protein** between the granulocyte colony-stimulating factor receptor (G- CSFR) and the **hormone-binding domain** (HBD) of the estrogen receptor (ER) as a selective amplifier gene. Use of the intracellular signaling pathway of G- CSFR was considered to be appropriate, because G-CSF has the ability not only to stimulate the neutrophil production, but also to expand the hematopoietic stem/progenitor cell pool in vivo. To activate the exogenous G-CSFR signal domain selectively, the estrogen/ER-HBD system was used as a molecular switch in this study. When the GCRER gene was expressed in the interleukin-3 (IL- 3)-dependent murine cell line, Ba/F3, the cells showed IL-3-independent growth in response to G-CSF or estrogen. Moreover, the Ba/F3 cells transfected with the Δ(5-195)GCRER, whose product lacks the extracellular G- CSF-binding domain, did not respond to G-CSF, but retained the ability for estrogen-dependent growth. Further, murine bane marrow cells transduced with the GCRER or Δ(5-195)GCRER gene with retroviral vectors formed a significant number of colonies in response to estrogen, as well as G-CSF, whereas estrogen did not stimulate colony formation by untransduced murine bone marrow cells. It is noteworthy that erythroid colonies were apparently formed by the bone marrow cells transduced with the GCRER gene in the presence of estrogen without the addition of erythropoietin, suggesting that the signals from the G-CSFR portion of the chimeric molecules do not preferentially induce neutrophilic differentiation, but just promote the differentiation depending on the nature of the target cells. We speculate that when the selective amplifier genes are expressed in the primitive hematopoietic stem cells, the growth signal predominates and that the population of transduced stem cells expands upon estrogen treatment, even if some of the cells enter the differentiation pathway. The present study suggests that this strategy is applicable to the in vivo selective expansion of transduced hematopoietic stem cells.

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